International Journal of Contemporary Pediatrics
Shirly Anitha GF et al. Int J Contemp Pediatr. 2016 Feb;3(1):288-290
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20160180

Case Report

A rare case of congenital leukemia: acute myeloblastic leukemia in a neonate with Down syndrome

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Received: 15 December 2015
Accepted: 11 January 2016

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ABSTRACT

Congenital leukemia is an exceedingly uncommon disease in newborn and is usually diagnosed at birth or within one month of life. It is usually associated with a fatal outcome. Neonates with Down syndrome have an increased risk of congenital leukemia. Because of the rapid doubling time of leukemic cells, the disease becomes clinically evident at birth or shortly thereafter. We report a case of congenital leukemia in a newborn with Down syndrome, the diagnosis of which was established with strong clinical suspicion and confirmed with haematological investigations.

Keywords: Congenital leukemia, Down syndrome

INTRODUCTION

Congenital leukemia is defined as leukemia that develops in utero. It is an extremely rare malignancy associated with grim prognosis and a poorly understood natural history.[1] Incidence is reported to be 1 per 5 million Neonates with down syndrome have a 20 fold increased risk of acute leukemia.[2,3] Only few cases of congenital leukemia with Down syndrome have been reported in the literature and here we report one such rare case.

CASE REPORT

A late preterm female neonate was delivered by LSCS at a government medical college hospital. The child was born of non-consanguineous marriage, mother's age 32, father's 35yrs and the antenatal period was uneventful. Birth weight was 2.3kg. The newborn had phenotypic features of Down syndrome with mongolian slant, low set ears, epicanthic folds, depressed nasal bridge, protruding tongue, saddle gap etc. (Figure 1-3). Baby was admitted in NICU for respiratory distress and was initially given oxygen through hood. Child was clinically pale and a detailed physical examination revealed a firm hepatosplenomegaly with liver 7cm below right costal margin, along with left lobe enlargement, spleen 2cm below left costal margin (Figure 4). Respiratory distress worsened after 3 hours of life; hence baby was intubated and put on mechanical ventilator support. With a firm hepatosplenomegaly and rapid deterioration in a newborn with Down phenotype, a clinical diagnosis of congenital leukemia was considered.

Lab investigations revealed total leucocyte count of 50,000/ mm^3 with predominant myeloblasts 91 % and a platelet count of 60,000/mm^3. Peripheral smear showed normocytic normochromic RBC morphology, thrombocytopenia and marked leucocytosis with blasts, no haemo parasites and an impression of Acute Myeloblastic leukemia was given. With a conclusive smear report samples for bone marrow aspiration and karyotyping were sent. Biochemical analysis showed a deranged liver function with AST 612 u/l, ALT 329u/l, alkaline phosphatase 316u/l; renal parameters were normal. Baby deteriorated with circulatory collapse, fluids and inotropes were administered, despite efforts the infant expired at 40hrs of life. The other reports were collected retrospectively and analysed. Bone marrow

aspiration revealed depressed erythropoiesis, myeloid hyperplasia, with myeloblasts constituting 70% of marrow nucleated cells; myeloblasts were granulated with occasional auer rods. Myeloid maturation was also noted and an impression of acute myeloblastic leukemia AML-M2 by morphology was made. Karyotyping confirmed trisomy 21. Culture reports were normal and TORCH screening was negative.

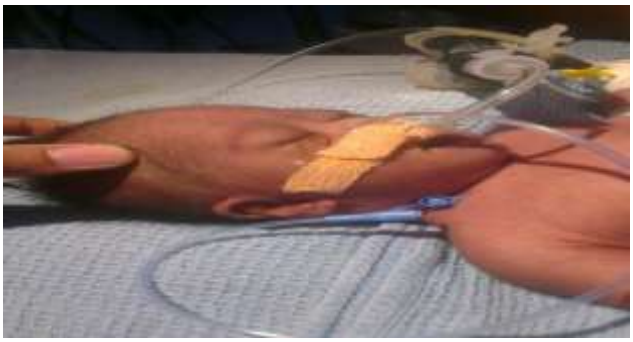

Figure 1: Facial dysmorphism.

Figure 2: Saddle gap.

Figure 3: On mechanical ventilator support.

DISCUSSION

Down syndrome is the most common chromosomal abnormality in a newborn. Haematological abnormalities in down range from non-fatal blood count abnormalities like polycythemia, leukopenia, neutropenia, thrombocytopenia to fatal conditions like leukemia and transient myeloproliferative disorder.[4] Congenital leukemia is an extremely rare disease in newborn. Criteria for diagnosis of congenital leukemia are: (a) disease presentation at or shortly after birth < 30 days. (b) proliferation of immature white cells (c) infiltration of cells in extra hematopoietic tissues (d) absence of any other condition that mimics congenital leukemia. Congenital leukemia is usually of myeloid origin in contrast to leukaemias in older age group which are usually lymphoid in origin. DS-AML in newborn usually presents with nodular skin infiltrates, hepatosplenomegaly, lethargy, poor feeding, pallor, purpura, petechiae, and respiratory distress. In a study of 6 cases of congenital leukemia, all of which were AML, autopsy showed leukemic infiltrates in lungs and other organs.[5] Most Down syndrome AML are of AML-M7 type whereas our case was AML-M2.

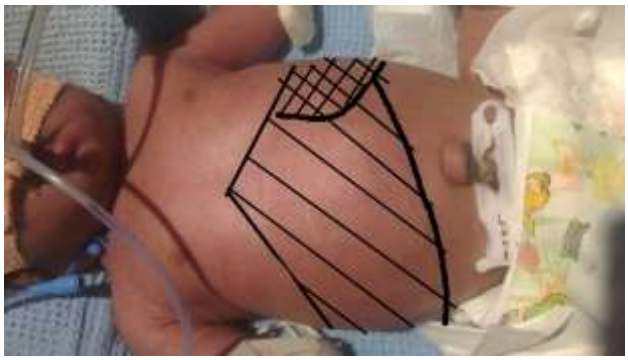

Figure 4: Hepatosplenomegaly-massive liver enlargement.

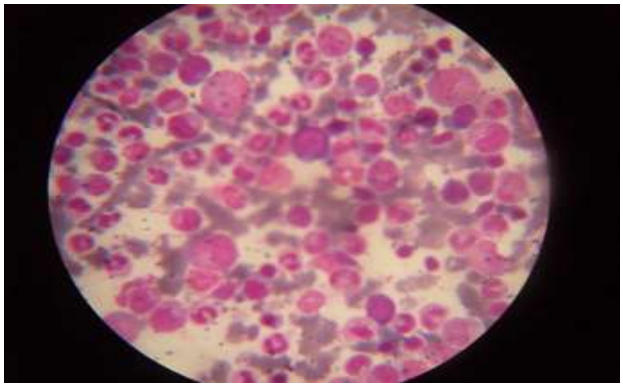

Figure 5: Bone marrow aspirate showing myeloblasts (high power).

Differential diagnosis

(a) Sepsis.
(b) TORCH infections.
(c) TMD – transient myeloproliferative disorder. Sepsis was ruled out by culture, TMD is associated with transient polycythemia, thrombocytosis and spontaneous resolution occurs within 3 months of onset.

CONCLUSION

The course of congenital leukemia is usually rapid deterioration and death from haemorrhage and infection. Studies have shown that children with Down syndrome respond well to chemotherapy and have a better outcome when compared to sporadic AML. Recent studies have identified a genetic mutation "GATA 1 mutation" associated in many patients of Down syndrome with TMD or leukemia. This mutation was found to be beneficial as it is responsible for greater sensitivity for specific chemotherapeutic drug cytosine arabinoside which contributes to greater survival rate.[6] This case is reported for its rarity and for classical clinical and haematological presentation of congenital leukemia.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Shirly Anitha GF, Danny Darlington C. A rare case of congenital leukemia: acute myeloblastic leukemia in a neonate with Down syndrome. Int J Contemp Pediatr 2016;3:288-90.